78. (Amended) The method of claim 33, wherein said PYY agonist ~~Therapeutic~~ enhances or recovers glucose responsiveness.

85. (Amended) The method of ~~any one of the above~~ claims 23, wherein said animal is a human.

REMARKS

Claims 1-13 and 15-91 constitute the pending claims in the present application. Claims 87-91 have been added. The subject matter of these claims is fully supported by the specification as filed. Claims 1-12, 24-27, 34-38, 40, 41, 44, 47-49, and 52 are withdrawn as being directed to a non-elected invention. Applicants will cancel such claims upon indication of allowable subject matter. Applicants submit, however, that claims 25-27, 34-37, 52, and 53-86 are properly dependent on elected independent claims and should be considered together upon determining that such independent claims are allowable, pursuant to MPEP 809.02(c). Accordingly, all of these claims are presented above. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Applicants gratefully acknowledge the withdrawal of objections to the specification and claims, as well as rejections under 35 U.S.C. § 112, second paragraph.

Claims 13, 15-23, 28-33, 39, 45, 46, 50, 51, 53, 54, 57-60, 63, 76-78, and 85 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Applicants have amended claim 85 to clarify the dependency. Applicants submit that the scope of the claim is not narrowed by this amendment.

Applicants have replaced the term 'PYY Therapeutic' throughout the claims with 'PYY agonist', thereby clarifying the function of this compound in light of the use of this term in passages from the specification as quoted the outstanding Office Action. Although the structure is not specified in the claims, the function is thus clarified sufficiently for one of skill in the art to recognize the scope of this term. Applicants submit that the only proper concern until 35 U.S.C.

§ 112, second paragraph, is whether one of skill in the art would recognize the metes and bounds of the term 'PYY agonist'. Given the clear definition of the functional attributes of PYY agonists in the specification, the many PYY agonists known in the art as exemplified by the Exhibits described in greater detail below, and the assays as described in the specification for characterizing PYY agonists, Applicants submit that this term is sufficiently clear to comply with 35 U.S.C. § 112, second paragraph.

Claims 21-23, 28-32, 39, and 50 are rejected for reciting "pharmaceutically effective amount". Applicants submit that this phrase does not appear in any of the above claims. Nevertheless, Applicants have adopted the Examiner's suggestion to clarify the meaning of the term "therapeutically effective amount". Applicants submit that the scope of these claims is not narrowed by this amendment.

For the reasons given above, Applicants submit that the pending claims are in full compliance with 35 U.S.C. §112, second paragraph. Reconsideration and withdrawal of this rejection is respectfully requested.

Claims 13-23, 28-33, 39, 45, 46, 50, 51, 53, 54, 57-60, 63, 76-78, and 85 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Applicants note that Exhibits A-C were unintentionally omitted from the previous response. Applicants apologize for this omission. Applicants respectfully request that the Examiner contact Applicants regarding any such omission in the future to expedite correction of such deficiencies.

The Office Action alleges that the specification is enabled for PYY but not for the broader class of PYY therapeutics. Applicants submit, however, that as of the filing date, a number of other PYY analogs were available, as indicated by the references and abstracts provided herewith as Exhibit A. Additionally, column 3 of U.S. Patent 5,574,010, incorporated by reference in the specification at the bottom of page 23, points out a number of other

references relating to compounds that fall within the scope of the term 'PYY agonists'. Although the Office Action argues that the method of treating pancreatic tumors is not predictive to the method claimed in this application, this argument is irrelevant to Applicants' argument. Applicants point to this patent not to demonstrate enablement of the treatment method *per se*, but rather to demonstrate that many PYY agonists were known to one skilled in the art at the time of filing of the present application, and that any of these would be expected to be efficacious in the claimed methods.

The art at the time of filing thus included a panoply of compounds that are 'PYY agonists' as this term is used in the specification and pending claims. Furthermore, one of ordinary skill in the art using assays described in these references could have identified any number of additional PYY agonists using only routine experimentation. Applicants respectfully remind the Examiner that "[a] patent need not teach, and preferably omits, what is well known in the art." MPEP 2164.01(a).

Applicants further direct the Examiner's attention to MPEP 2164.04. This section delineates the Examiner's burden "to establish a reasonable basis to question the enablement provided for the claimed invention." Specifically, "it is incumbent upon the Patent Office, whenever a rejection on this basis, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *In re Marzocchi*, 169 USPQ 367, 370 (CCPA 1971). Additionally, the Federal Circuit recently articulated a standard whereby the PTO must establish a rational connection between the agency's fact-findings and its ultimate action. *Dickinson v. Zurko*, 119 S.Ct. 1816 (1999). In light of the Applicants' arguments of record, and the presumption in favor of Applicants, it is respectfully asserted that the present rejection is not supported by substantial evidence, and as such, fails to rise above the "arbitrary, capricious" standard applied under the "substantial evidence" test of Section 706(2)(E) of the Administrative Procedure Act. The Examiner has not cited any relevant art nor relied on any other fact-finding results to rebut the presumption in favor of Applicants. Accordingly, Applicants submit that the use of 'PYY agonists' is fully enabled by the present specification and the level of skill in the art at the time of filing of the present application.

Lastly, the Office Action questions whether the *in vitro* results disclosed in the application would have been expected to function similarly *in vivo*. The Examiner has cited art suggesting that such correlation is unreliable. None of this art, however, relates to PYY Therapeutics in particular. Applicants submit herewith as Exhibit **B** a selection of abstracts that demonstrate that *in vivo* and *in vitro* functions of PYY show a strong correlation. For example, the abstract of Souli et al., *Peptides* **1997**, *18*, 551-557, teaches the correspondence of *in vivo* and *in vitro* results using PYY to inhibit VIP-induced fluid secretion in rat jejeunum. Balasubramanian et al., *J. Med. Chem.* **2000**, *43*, 3420-3427, demonstrate that a variety of PYY analogs that exhibit *in vitro* activity are also active *in vivo* in the intestine of dogs. Grise et al., *J. Surg. Res.* **1999**, *82*, 151-155, show that PYY inhibits growth of breast cancer *in vivo* and *in vitro* alike. Bertrand et al., *Pancreas* **1992**, *7*, 595-600, extend this correlation even to the insulin secretion functions of the pancreas. In light of these favorable results relating to the particular therapeutics contemplated by the present invention, Applicants submit that the generalized teachings cited by the Examiner fail to undermine the enablement of the presently claimed methods. Applicants submit that the knowledge in the art demonstrates a reasonable correlation between *in vivo* and *in vitro* results using PYY therapeutics that supports enablement of the pending claims. These results also counter the generalized concerns raised by the Examiner relating to biological stability, immunological activation, bioavailability, etc., as the successful use of PYY *in vivo* to affect various organs including the pancreas is clearly demonstrated by these abstracts. Nevertheless, Applicants have amended the claims to recite "PYY agonist" in place of "PYY therapeutic". Reconsideration and withdrawal of this rejection are respectfully requested.

In addition, Applicants submit herewith as Exhibit **C** selected pages from a continuation-in-part (U.S. Application No. 09/634,363, filed August 9, 2000) of the present application, which relates to successful use of PYY *in vivo* results to control glucose levels in rats predisposed to diabetes. These results indicate that the claimed methods, as disclosed in the present application, would have been effective as taught by Applicants at the time of filing. For all of the above reasons, which demonstrate that the present claims were enabled throughout their scope at the time of filing, reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the pending rejections. Applicants believe that the claims are now in condition for allowance and early notification to this effect is earnestly solicited. Any questions arising from this submission may be directed to the undersigned at (617) 951-7000.

If there are any other fees due in connection with the filing of this Reply, please charge the fees to our **Deposit Account No. 18-1945.** If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit account.

Respectfully Submitted,

Date: November 27, 2001

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